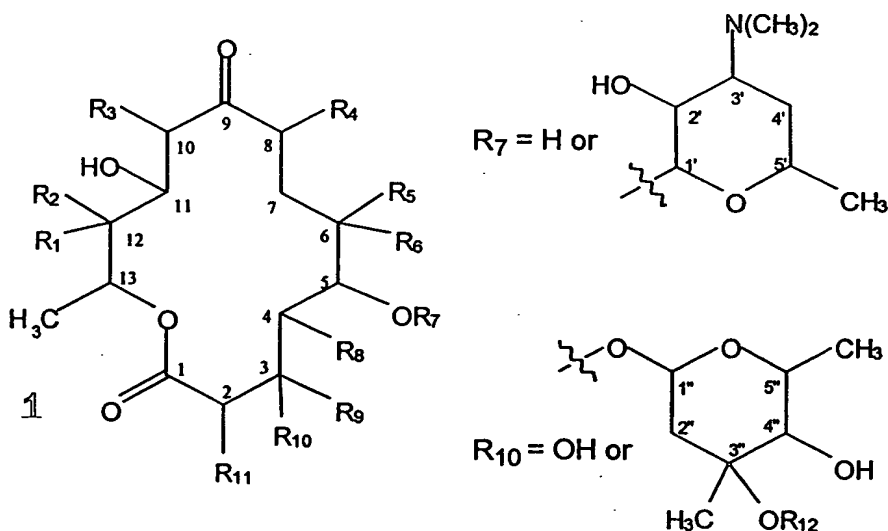


Claims

1. A 14-member macrolide which incorporates an acetate starter unit so that it has a 13-methyl substituent, with the proviso that it is not  
 5 norerythromycin C, 6-deoxy-15-norerythromycin B or 6-deoxy-15-norerythromycin D.
2. 15-norerythromycin A.
- 10 3. 15-norerythromycin B.
4. A compound of the formula 1:



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or a pharmaceutically acceptable salt thereof, wherein:

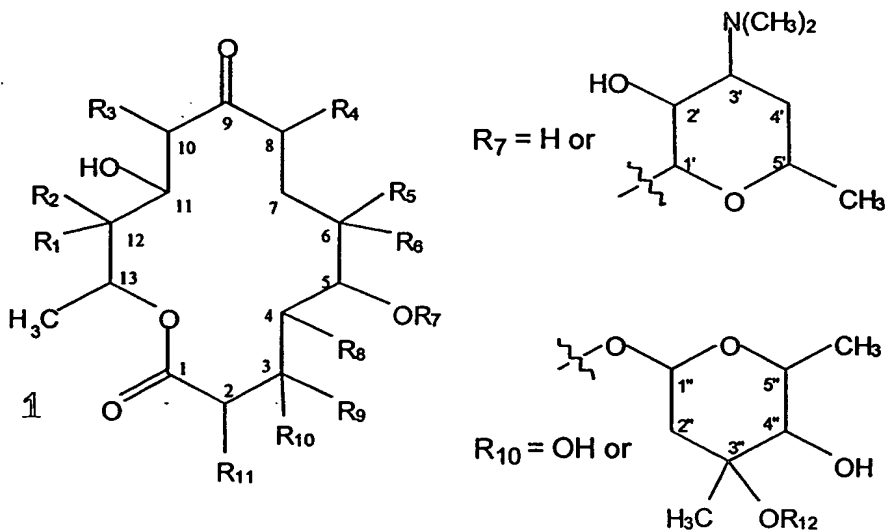
$R_1$  is H or OH;  $R_2$ - $R_4$  are each independently H,  $\text{CH}_3$ , or  $\text{CH}_2\text{CH}_3$ ;  $R_5$  is H or OH; and  $R_6$  is H,  $\text{CH}_3$ , or  $\text{CH}_2\text{CH}_3$ ;  $R_7$  is H or desosamine;  $R_8$  is H,  $\text{CH}_3$ , or  $\text{CH}_2\text{CH}_3$ ;  $R_9$  is OH, mycarose  
 20 ( $R_{12}$  is H), or cladinose ( $R_{12}$  is  $\text{CH}_3$ ),  $R_{10}$  is H; or  $R_9 = R_{10}$

= O; and  $R_{11}$  is H,  $\text{CH}_3$ , or  $\text{CH}_2\text{CH}_3$ , with the proviso that when  $R_2$ - $R_4$  are  $\text{CH}_3$ ,  $R_6$  is  $\text{CH}_3$ ,  $R_8$  is  $\text{CH}_3$ , and  $R_{11}$  is  $\text{CH}_3$ , then  $R_1$  and  $R_5$  are not H and  $R_{12}$  is not H; or also when  $R_2$ - $R_4$  are  $\text{CH}_3$ ,  $R_6$  is  $\text{CH}_3$ ,  $R_8$  is  $\text{CH}_3$ , and  $R_{11}$  is  $\text{CH}_3$ , then  $R_1$  and  $R_5$  are not OH and  $R_{12}$  is not H.

5. A compound according to claim 4 wherein  $R_1$  is OH;  $R_2$ - $R_4$  are  $\text{CH}_3$ ;  $R_5$  is OH;  $R_6$  is  $\text{CH}_3$ ,  $R_7$  is desosamine;  $R_8$  is  $\text{CH}_3$ ;  $R_9$  is cladinose ( $R_{12}$  is  $\text{CH}_3$ ); and  $R_{11}$  is  $\text{CH}_3$

6. A compound according to claim 4 wherein  $R_1$  is H;  $R_2$ - $R_4$  are  $\text{CH}_3$ ;  $R_5$  is OH;  $R_6$  is  $\text{CH}_3$ ,  $R_7$  is desosamine;  $R_8$  is  $\text{CH}_3$ ;  $R_9$  is cladinose ( $R_{12}$  is  $\text{CH}_3$ ); and  $R_{11}$  is  $\text{CH}_3$ .

7. A process for making compounds of the formula 1:



wherein:

$R_1$  is H or OH;  $R_2$ - $R_4$  are each independently H,  $\text{CH}_3$ , or  $\text{CH}_2\text{CH}_3$ ;  $R_5$  is H or OH; and  $R_6$  is H,  $\text{CH}_3$ , or  $\text{CH}_2\text{CH}_3$ ;  $R_7$  is H or desosamine;  $R_8$  is H,  $\text{CH}_3$ , or  $\text{CH}_2\text{CH}_3$ ;  $R_9$  is OH, mycarose

(R<sub>12</sub> is H), or cladinose (R<sub>12</sub> is CH<sub>3</sub>), R<sub>10</sub> is H; or R<sub>9</sub> = R<sub>10</sub> = O; and R<sub>11</sub> is H, CH<sub>3</sub>, or CH<sub>2</sub>CH<sub>3</sub>

8. A process for making compound of the formula 1 as set out in claim 7 wherein R<sub>1</sub> is OH; R<sub>2</sub>-R<sub>4</sub> are CH<sub>3</sub>; R<sub>5</sub> is OH; R<sub>6</sub> is CH<sub>3</sub>, R<sub>7</sub> is desosamine; R<sub>8</sub> is CH<sub>3</sub>; R<sub>9</sub> is cladinose (R<sub>12</sub> is CH<sub>3</sub>); and R<sub>11</sub> is CH<sub>3</sub>

9. A process for making compound of the formula 1 as set out in claim 7 wherein R<sub>1</sub> is H; R<sub>2</sub>-R<sub>4</sub> are CH<sub>3</sub>; R<sub>5</sub> is OH; R<sub>6</sub> is CH<sub>3</sub>, R<sub>7</sub> is desosamine; R<sub>8</sub> is CH<sub>3</sub>; R<sub>9</sub> is cladinose (R<sub>12</sub> is CH<sub>3</sub>); and R<sub>11</sub> is CH<sub>3</sub>

10. A system for producing a 14-membered macrolide incorporating an acetate starter unit, said system comprising DNA encoding and arranged to express a PKS multienzyme which comprises a loading module and a plurality of extension modules; wherein in the expressed multienzyme, said loading module is adapted to load a malonyl residue and then to effect a decarboxylation of the loaded residue to provide an acetate starter unit which is transferred to an adjacent one of said extension modules; and wherein the extension modules, or at least one thereof, are not naturally associated with a loading module that effects decarboxylation.

11. A system according to claim 10 wherein the macrolide is a compound of formula 1 as defined in any of claims 4-9.

12. A system according to claim 10 or 11 wherein said adjacent extension module to which the acetate starter is transferred is not naturally associated with a loading  
5 module that effects decarboxylation.

13. A system according to claim 10, 11 or 12 wherein the decarboxylating functionality of the loading module is provided by a ketosynthase-type domain having a glutamine  
10 residue in the active site.

14. A system according to claim 10, 11 or 12 wherein the decarboxylating functionality of the loading module is provided by a CLF-type domain.

15. A system according to claim 14 wherein the CLF-type domain is substantially as any shown in Fig 2.

16. A system according to any of claims 10-15 wherein  
20 the loading module's loading functionality is provided by an acyltransferase-type domain having an arginine residue in the active site.

17. A system according to any of claims 10-16 wherein  
25 the loading module includes an acyl carrier protein.

18. A system according to any of claims 10-13, 16 or 17 wherein at least the KS<sub>Q</sub> domain of said loading module corresponds to the loading module of the PKS multienzyme of oleandomycin, spiramycin, niddamycin, methymycin, or monensin.
19. A PKS multienzyme as expressible by the DNA of the system of any of claims 10-18 or a variant having the ability to synthesise a compound of formula 1.
20. Nucleic acid encoding the PKS multienzyme of claim 19.
21. A vector containing nucleic acid as defined in claim 20.
22. A transformant organism comprising a system according to any of claims 10-18.
23. A process according to claim 7, 8, or 9 which comprises culturing an organism according to claim 22 and recovering a compound of formula 1.
24. A process according to claim 23 wherein said macrolide is a compound of formula 1 as defined in any of claims 4-9.

25. A system, organism or process according to any of  
claims 10-24 wherein the plurality of extension modules  
corresponds to the extension modules of a PKS selected  
5 from erythromycin, narbomycin, pikromycin, lankamycin,  
kujimycin or megalomycin or a mutant or variant thereof  
able to direct synthesis of a macrolide.